Yellow Fever

Section 1: ABOUT THE DISEASE

A. Etiologic Agent

Yellow fever is a mosquito-borne viral illness. It is caused by the yellow fever virus, which is in the genus *Flavivirus* and the family *Flaviviridae*.

B. Clinical Description

Many cases of yellow fever are mild and go undetected. In typical cases of recognized illness, the patient experiences a sudden onset of fever, chills, headache, backache, generalized muscle pain, prostration, nausea, and vomiting. Jaundice, albuminuria (the presence of protein in the urine), and anuria (absence of urine) may occur. Most infections resolve at this stage. However, in more severe cases of illness, after a brief remission lasting from hours up to a day, there is progression to liver and kidney failure and to hemorrhagic symptoms, including nosebleeds, bleeding gums, bloody vomiting (hematemesis), and bloody stools. Of severe cases with jaundice, 20-50% are fatal. The overall case-fatality rate in endemic regions is about 5%. Lifetime immunity to yellow fever follows recovery.

C. Vectors and Reservoirs

Monkeys and mosquitoes are the primary reservoirs in forested areas of Africa and South America. Humans and *Aedes aegypti* mosquitoes are involved in the infective cycle in urban areas. Mosquitoes are the vector for transmission.

D. Modes of Transmission

Yellow fever is mosquito-borne and has two different transmission cycles that affect humans: the urban cycle and the jungle cycle. In the urban cycle, the virus is transmitted among humans by the bite of an infective house-dwelling *A. aegypti* mosquito. Monkeys play little or no role as a reservoir. In the jungle cycle, several species of mosquitoes are vectors, and they transmit the virus from monkey to monkey. Humans are involved in the jungle cycle coincidentally if they are bitten by infected mosquitoes. In South America, sporadic infection of humans occurs almost exclusively in forestry and agricultural workers through occupational exposure. Direct person-to-person spread of yellow fever does not occur.

Note: The A. aegypti mosquito has not been found in Massachusetts, although it and other vectors are expanding their range. Concerns over local transmission should be extremely low.

E. Incubation Period

The incubation period for yellow fever is 3-6 days.

F. Period of Communicability or Infectious Period

Yellow fever is not transmitted directly from person to person. People infected with yellow fever are considered infectious to mosquitoes from shortly before onset of fever to the end of the febrile period, usually about 3–5 days. The mosquito becomes infective 9–12 days after a blood meal from an infectious person or monkey, and it remains infective for its lifetime.

G. Epidemiology

Yellow fever is now endemic only in certain regions of South America and in Africa. In Massachusetts, yellow fever may be identified in people who have recently traveled to an endemic area.

H. Bioterrorist Potential

This pathogen is not considered to be of risk for use in bioterrorism.

Section 2:
REPORTING CRITERIA AND LABORATORY TESTING

A. What to Report to the Massachusetts Department of Public Health (MDPH)

Report any suspect case of yellow fever based on a health care provider's medical opinion or any positive laboratory result pertaining to yellow fever.

Note: See Section 3C for information on how to report a case.

B. Laboratory Testing Services Available

The MDPH State Laboratory Institute (SLI) does not provide testing services for yellow fever virus. However, the SLI Virus Serology Laboratory can arrange for serum samples to be forwarded to the Centers for Disease Control and Prevention (CDC) for testing. Specimens should be submitted with a complete case history.

For additional information on testing or specimen submission, contact the SLI Virus Serology Laboratory at (617) 983-6396. Please call the laboratory prior to specimen submission.

Section 3:
REPORTING RESPONSIBILITIES AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- To identify imported cases of yellow fever to understand the global epidemiology of endemic and epidemic yellow fever.
- To ensure that cases are appropriately contained to prevent the introduction of virus into native mosquito populations.

- To identify locally acquired cases, if they occur, so appropriate active surveillance and mosquito control interventions can be taken.
- To identify cases that may be part of a larger, worldwide outbreak.
- To provide travelers with appropriate preventive health information.

B. Laboratory and Health Care Provider Reporting Requirements

Yellow fever is reportable to the local board of health (LBOH). The MDPH requests that health care providers immediately report to the LBOH in the community where the case is diagnosed, all confirmed or suspect cases of yellow fever, as defined by the reporting criteria in Section 2A.

Laboratories performing examinations on any specimens derived from Massachusetts residents that yield evidence of yellow fever infection shall report such evidence of infection directly to the MDPH within 24 hours.

C. Local Board of Health (LBOH) Reporting and Follow-Up Responsibilities

Reporting Requirements

MDPH regulations *(105 CMR 300.000)* stipulate that yellow fever is reportable to the LBOH and that each LBOH must report any case of yellow fever or suspect case of yellow fever, as defined by the reporting criteria in Section 2A. Cases should be reported to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS) using an official MDPH *Arbovirus Case Report Form* (found at the end of this chapter). Refer to the *Local Board of Health Timeline* at the end of this manual's *Introduction* section for information on prioritization and timeliness requirements of reporting and case investigation.

Case Investigation

Case investigation of yellow fever in Massachusetts residents will be directed by the MDPH Division of Epidemiology and Immunization.

1. Following notification of the MDPH, the LBOH may be asked to assist in completing an official MDPH *Arbovirus Case Report Form* (found at the end of this chapter). Most of the information required on the form can be obtained from the health care provider or from the medical record. Use the following guidelines to assist in completing the form:
   a. Demographic information: Accurately record the case's age, sex, race, occupation, and contact information.
   b. Clinical information: Note the symptom onset date and check off all reported symptoms. Also note whether the case is pregnant. Record whether the case was hospitalized, including location, associated dates, and physician contact information.
   c. Laboratory information: Check off all appropriate tests performed and attach a copy of any laboratory results.
   d. Information relevant to control and prevention: It is extremely important to record the case's travel history by determining the date(s) and geographic area(s) of travel within 30 days prior to onset. Also complete the vaccination and disease history sections. It is very important to determine whether the individual had been

previously vaccinated for yellow fever. If the individual has been previously vaccinated for yellow fever, note the date in the "Comments" section.

e. Include any additional comments regarding the case.

f. If you have made several attempts to obtain case information but have been unsuccessful (e.g., the case or health care provider does not return your calls or respond to a letter, or the case refuses to divulge information or is too ill to be interviewed), please fill out the form with as much information as you have gathered. Please note on the form the reason(s) why it could not be filled out completely.

2. After completing the form, attach laboratory report(s) and fax or mail (in an envelope marked "Confidential") to ISIS. The confidential fax number is (617) 983-6813. Call ISIS at (617) 983-6801 to confirm receipt of your fax. The mailing address is:

MDPH, Office of Integrated Surveillance and Informatics Services (ISIS)
305 South Street, 5th Floor
Jamaica Plain, MA 02130
Fax: (617) 983-6813

3. Institution of disease control measures is an integral part of case investigation. It is the responsibility of the LBOH to understand, and if necessary, institute the control guidelines listed in Section 4.

Section 4:
CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements *(150 CMR 300.200)*

No restrictions. While there are no required restrictions, cases should avoid exposure to mosquitoes for at least five days after onset of illness in order to prevent spread of yellow fever virus to local mosquito populations. See Section 4D for more information.

Note: The A. aegypti mosquito has not been found in Massachusetts, although it and other vectors are suspected of expanding their range. Concern over local transmission should be low.

B. Protection of Contacts of a Case

No restrictions.

C. Managing Special Situations

Locally-Acquired Case

As noted in Section 4B, a locally-acquired case of yellow fever would be an unusual occurrence as the *A. aegypti* mosquito has not been found in Massachusetts. However, in recent years, a resurgence of *A. aegypti* has occurred in South America and has increased the potential for the reemergence of urban yellow fever (see Section 1D for a description of urban yellow fever) in the U.S. If you determine during the course of an investigation that a case or suspect case does not have a recent travel history to an endemic country, contact the epidemiologist on-call at the

MDPH Division of Epidemiology and Immunization, at (617) 983-6800 or (888) 658-2850, as soon as possible. Investigation of local areas visited by the case to locate the focus of infection and to conduct surveillance of other people for illness may be necessary.

Reported Incidence Is Higher Than Usual/Outbreak Suspected

If the number of reported cases of yellow fever in your city/town is higher than usual or if you suspect an outbreak, investigate to determine the source of infection and the mode of transmission. A common exposure to or association with *A. aegypti* mosquitoes (e.g., travelers returning from endemic countries) should be sought, and applicable preventive or control measures should be instituted. Contact the epidemiologist on-call at the MDPH Division of Epidemiology and Immunization, at (617) 983-6800 or (888) 658-2850, as soon as possible. The Division can help determine a course of action to prevent further cases and can perform surveillance for cases across town lines, which would otherwise be difficult to identify at the local level.

D. Preventive Measures

International Travel and Vaccination

A live vaccine is recommended for individuals who will be living in or traveling to endemic areas and is required by international regulations for travel to and from certain countries. Complete information on vaccine administration, as well as contraindications, may be obtained from the manufacturer's vaccine product insert. In general, the vaccine should not be administered to infants under nine months of age, to pregnant women, to individuals with certain immunosuppressive conditions, and to individuals who are hypersensitive to eggs. The vaccine should be avoided by women who are breastfeeding.

Without a valid certificate of immunization against yellow fever, many countries require a six-day quarantine of travelers coming from or going to recognized yellow fever zones of Africa and South America.

Travelers to yellow fever endemic countries can protect themselves from mosquitoes by using repellents that contain DEET, by wearing protective clothing, and by using mosquito nets when rooms are not screened.

When using repellents containing DEET (N,N-diethyl-m-toluamide), choose a product that will provide sufficient protection for the amount of time spent outdoors. Product labels often indicate the length of time that someone can expect protection from a product. DEET is considered safe when used according to the manufacturer's directions. The efficacy of DEET levels off at a concentration of 30%, which is the highest concentration recommended for children and adults. DEET products should not be used on children less than two months of age. Mosquito netting may be used to cover infant carriers or to protect other areas for children less than two months of age. The following precautions should be observed when using DEET products:

- Avoid using DEET products that combine the repellent with a sunscreen. Sunscreens may need to be reapplied too often, resulting in an over-application of DEET.
- Apply DEET on exposed skin, using only as much as needed.
- Do not use DEET on the hands of young children, and avoid applying repellent to areas around the eyes and mouth.
- Do not use DEET over cuts, wounds, or irritated skin.
- Wash treated skin with soap and water after returning indoors, and wash treated clothing.
- Avoid spraying DEET products in enclosed areas.

Picardin (KBR 3023) is a relatively new repellent that is now available in the U.S. Recent studies have shown it to be safe and effective against mosquitoes. Picardin-containing repellents should be used according to the manufacturer's recommendations.

Permethrin-containing products will kill mosquitoes and ticks on contact. Permethrin products are not designed to be applied to the skin. Clothing should be treated and allowed to dry in a well-ventilated area prior to wearing. Because permethrin binds very tightly to fabrics, once the fabric is dry, very little of the permethrin gets onto the skin.

A number of plant-derived products are available for use as repellents, but most of these products do not provide the same level or duration of protection as products containing DEET. However, there are studies that show that oil of lemon eucalyptus (p-methane 3,8-diol[PMD]) provides as much protection as low concentrations of DEET when tested against mosquitoes found in the U.S.

Unlike other vectors, the principal mosquito vectors of yellow fever bite during daytime hours.

Note: For more information regarding international travel and the yellow fever vaccine, contact the CDC's Traveler's Health Office at (877) 394-8747 or on the CDC website at www.cdc.gov/travel.

ADDITIONAL INFORMATION

The following is the formal CDC surveillance case definition for yellow fever. It is provided for your information only and should not affect the investigation and reporting of a case that fulfills the criteria in Section 2A of this chapter. (The CDC and the MDPH use the CDC case definitions to maintain uniform standards for national reporting.) For reporting to the MDPH, always use the criteria outlined in Section 2A.

Note: The most up-to-date CDC case definitions are available on the CDC website at www.cdc.gov/epo/dphsi/casedef/case_definitions.htm.

Clinical Description

A mosquito-borne viral illness characterized by acute onset and constitutional symptoms, followed by a brief remission and a recurrence of fever, hepatitis, albuminuria, and in some instances, renal failure, shock, and generalized hemorrhages.

Laboratory Criteria for Diagnosis

- Four-fold or greater rise in yellow fever antibody titer in a patient who has no recent history of yellow fever vaccination and cross-reactions to other flaviviruses have been excluded; or
- Demonstration of yellow fever virus, antigen, or genome in tissue, blood, or other body fluid.

Case Classification

Probable	A clinically-compatible case with supportive serology (stable elevated antibody to yellow fever virus [e.g., ≥32 by complement fixation, ≥256 by immunofluorescence assay, ≥320 by hemagglutination inhibition, ≥160 by neutralization, or a positive serologic result by immunoglobulin M-capture enzyme immunoassay]. Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of yellow fever vaccination.)
Confirmed	A clinically-compatible case that is laboratory-confirmed.

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FORMS & WORKSHEETS

Yellow Fever

Yellow Fever

LBOH Action Steps

This form does not need to be submitted to the MDPH with the case report form. It is for LBOH use and is meant as a quick-reference guide to yellow fever case investigation activities.

LBOH staff should follow these steps when yellow fever is suspected or confirmed in the community. For more detailed information, including disease epidemiology, reporting, case investigation and follow-up, refer to the preceding chapter.

- ❑ Notify the MDPH Division of Epidemiology and Immunization, at (617) 983-6800 or (888) 658-2850, to report any suspect or confirmed case(s) of yellow fever.
- ❑ Assist MDPH with obtaining clinical specimens needed for laboratory confirmation, if necessary.
- ❑ Determine whether or not the case was acquired locally, and if so, conduct enhanced surveillance for human illness and investigate local risk factors for viral transmission.
- ❑ If locally acquired, institute mosquito control measures.
- ❑ Fill out a MDPH *Arbovirus Case Report Form* (attach laboratory results). Be sure to obtain an accurate travel history.
- ❑ Send the completed case report form (with laboratory results) to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS).